

AUTOTRANSPLANTATION IN LINGUAL ECTOPIA OF THE THYROID GLAND*

REVIEW OF THE LITERATURE AND REPORT OF A SUCCESSFUL CASE

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Though 'lingual thyroid' has been an accepted term for many years, precise terminology might be served better by the use of ectopia to indicate those cases—the majority—in which no thyroid tissue exists in the orthotopic (prelaryngeal) site, the prefix lingual indicating the site of ectopia. Ectopia also serves to describe the situation in which a 'thyroglossal cyst' is solid and represents the only thyroid tissue which the patient possesses. Such cases are analogous to lingual ectopia, the difference lying in the point at which migration is arrested. If this designation is accepted, the term 'aberrant thyroid' could be reserved for those cases in which orthotopic thyroid tissue coexists.

The introduction of radioactive iodine I^{131} uptake surveys has made it possible to determine the exact site or sites of functioning thyroid tissue, and has displaced both biopsy of ectopic lingual tissue and cervical exploration for orthotopic thyroid.

Since Hickman (1869) described the first case, experience of lingual ectopia of the thyroid gland has steadily accumulated and there are now over 200 cases on record. Montgomery (1936) in a critical review suggested criteria for authenticity and at that time accepted 144 cases as proven. His criteria were:

1. A lingual tumour situated between the epiglottis and the circumvallate papillae.
2. Biopsy of the tumour demonstrating the presence of thyroid tissue.
3. As an alternative, the supervention of a hypothyroid state on operative removal of the tumour.

Clinical signs or symptoms have appeared during puberty or adolescence in almost half of the cases recorded. They can be summarized as follows:

1. The most common symptoms were those of oropharyngeal obstruction, e.g. dysphagia, dysarthria, dyspnoea, orthopnoea.
2. Haemorrhage, often recurrent and in small

amounts, occurred from dilated submucous venules on the surface of the lingual mass.

3. Disturbances of thyroid function.

Montgomery's series contained four cases showing features of hyperthyroidism and 21 of hypothyroidism.

Oral examination reveals a pink, grey or red swelling looming over the horizon of the tongue, which is best seen with the aid of traction and depression of the tongue.

In contemporary practice radioactive iodine I^{131} 'uptake' survey is the most valuable investigatory procedure, for it confirms or disproves the diagnosis and indicates the presence or absence of orthotopic thyroid tissue.

Case Report

A 9-year-old girl was referred for consultation in June, 1958, because of a tumour and respiratory obstruction noted during anaesthesia and tonsillectomy; this had been undertaken for snoring and mouth breathing. Her mother had noticed a change in the girl's voice, huskiness and dysarthria becoming more marked over a period of two years. Recently mild dysphagia had appeared and noisy mouth breathing was present during sleep. The patient had lived in Traralgon all her life, an area of Victoria recognized as goitrogenic. Iodized domestic salt had been used in the household, this being the common practice in the region. Her health in the past had been good and there was no other relevant history.

General examination showed a solidly-built and normally developed prepubertal girl, the only apparent physical abnormality being a reddish spherical tumour projecting above the dorsum of the tongue in the region of the foramen caecum. There was a peculiar empty feeling between the sternomastoid muscles and the thyroid cartilage.

Investigation. On July 7, 1958, a tracer dose of 5.8 μ c. of I^{131} was administered orally, and followed 24 hours later by scintillometry which showed that I^{131} was concentrated in the region of the base of the tongue approximately 8 cm. above the sternal notch. There was no

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

significant uptake in the normal thyroid region. The 24-hour retention of I^{131} in the lingual area was 60% of the oral dose. Surgical treatment was decided upon. Oral tetracycline (250 mg.) and penicillin (250 mg.) were administered at six-hour intervals commencing two days before operation on July 16. Premedication of inj. papaveritum (10 mg.) with L-hyoscine hydrobromide (0.2 mg.) was given 45 minutes before anaesthesia which was induced with intravenous thiopentone (200 mg.) augmented with nitrous oxide, oxygen and halothane mixture. Two injections of 'scoline', succinylcholine chloride (50 mg.) were necessary to achieve per-nasal intubation of the larynx, performed 'blind' by fingertip touch guidance. The tumour prevented the introduction of a laryngoscope. Anaesthesia was then continued with 1.3% halothane in nitrous oxide and oxygen mixture.

Operation. When the tongue was forcefully drawn forwards with several chromic sutures, the swelling was still inaccessible. Right lateral pharyngotomy was chosen as the alternative route, as the tumour extended more towards this side (Fig. 1). A slightly curved incision was made over the submandibular area (Fig. 2); the platysma and fascia were divided in the line of the incision and reflected upwards with the unidentified cervical branch of the facial nerve. The anterior facial vein and facial artery were divided and the submandibular gland excised, the deep portion of the gland being withdrawn from beneath mylohyoid muscle, and the submandibular duct severed after identifying the lingual nerve (Fig. 3).

The intermediate tendon of the digastric muscle was then divided, and the posterior belly turned laterally to display the greatly enlarged and tortuous lingual artery (Fig. 4).

By dividing the hyoglossus muscle, with its nerve supply, and retracting both lingual and hypoglossal nerves cranially, the pharyngeal wall and middle constrictor of the pharynx were displayed (Fig. 5).

The pharynx was opened by an oblique curved incision giving the exposure indicated in Fig. 6 which has been interpreted with some licence to permit orientation.

Pressure exerted by an assistant's finger in the mouth dislocated the mass into the incision (Fig. 7). As no plane of cleavage existed between tumour and tongue, scissor dissection and suture ligatures were necessary to free the inferior and anterior aspects.

Haemostasis and closure of the depression in the tongue were effected by atraumatic chromic sutures. The front of the epiglottis had been denuded of mucous membrane and the possibility of postoperative oedema in the area was considered sufficient indication for tracheostomy.

Reconstitution of each stratum was performed, and a small roll of dental dam drain led from the closed pharyngeal wall incision to the exterior through a small separate stab.

Transplantation was commenced during closure of the cervical incision. The excised mass was denuded of mucous membrane, cut into slices and then 2.3 mm. cubes. A transverse lower abdominal incision was made

and the anterior rectus sheath opened vertically. Tissue in the rectus muscle fibres at first ejected the cubes of tissue until a further 50 mg. of succinylcholine chloride were administered. The relaxed rectus fibres were parted and groups of 5-6 cubes were inserted at several points, totalling approximately 150 mm.³ of thyroid tissue. A fine catgut suture was placed across each group of parted muscle fibres to retain the cubes in position.

Tracheostomy was then performed, the cannula insertion being synchronous with anaesthetic extubation.

Microscopy. Sections of the ectopic thyroid gland showed a preponderance of foetal adenoma pattern, with a few scattered areas of colloid formation (Fig. 8). The macroscopic specimen had been hastily sliced for transplantation and there was inadequate material for a complete examination of the base of the tumour and its relation to the underlying muscle of the tongue.

Postoperative Course. The postoperative course was uneventful apart from muscular weakness of the right angle of the mouth which recovered in six weeks. The tracheostomy in retrospect was found to have been unnecessary, and the cannula was removed on the fifth postoperative day. All sutures were removed by the seventh day, and chemotherapy was discontinued at this time. Twelve days after operation a basal metabolic rate (B.M.R.) estimation was -24 and the serum cholesterol level was 380 mg. per 100 ml. This coincided with a temporary clinical picture of a mild hypothyroid state. She gained weight and appeared quiet and lethargic. This may have been in part a reaction to her experiences in hospital.

Scintillometry was repeated five weeks after operation and showed that a very small amount of I^{131} (some 4.5% of the oral dose) was concentrated in the lingual region. This count was obtained in the midline 8 cm. above the sternal notch. In the region of the autograft there was an uptake of the order of 20% of the total dose of 10 μ c. A B.M.R. estimation at this time was -8 and a reading one month later was +8. This corresponded with a definite improvement in the patient's general appearance and suggested probable return to a euthyroid state. There was thus strong evidence that the autografted tissue was functioning within five weeks of operation and after a period of mild hypothyroidism. No thyroid substitutes were administered at any time.

She was reviewed at the age of 11 years in April 1960, when the tongue was normal. Puberty was well advanced and though no menarche had occurred, breast and pubic hair development were virtually adult in degree. A B.M.R. estimation was +1; serum cholesterol, 312 mg. %; serum alkaline phosphatase, 23 Wohlgemuth units; her radiographic epiphyseal age was normal. Electrocardiography showed low voltage complexes possibly compatible with mild hypothyroidism.

An estimation of protein-bound iodine (P.B.I.) was 4.8 μ g. (normal range 3.0-7.5 mg. %). A course of thyroid stimulating hormone (T.S.H.) was then administered as Organon Laboratory 'Ambinon B', an unstandardized mixture of T.S.H. and gonadotropins. Four

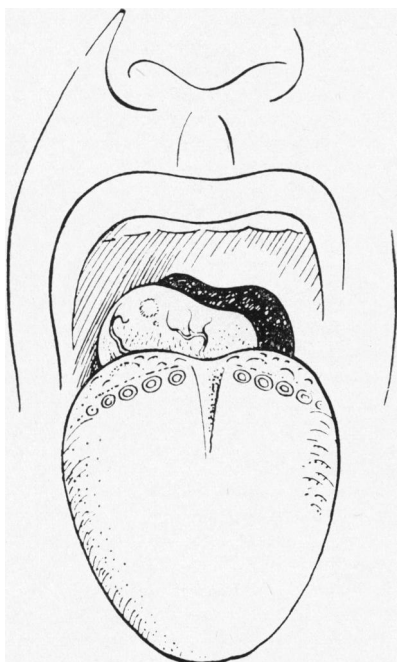


FIG. 1.—The lesion in the mouth with full traction on the tongue

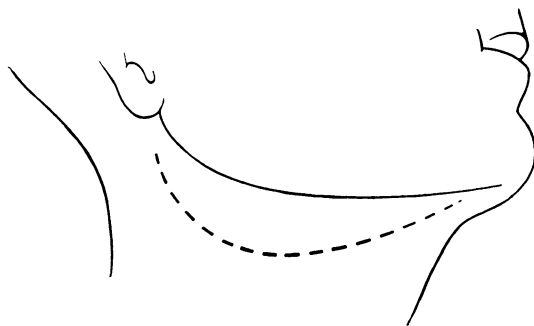


FIG. 2.—The incision.

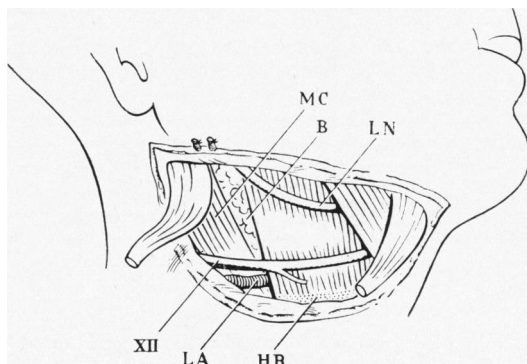


FIG. 4.—The floor of the digastric triangle.

MC: Middle constrictor muscle.
 B: Buccopharyngeal fascia.
 LN: Lingual nerve.
 XII: Hypoglossal nerve and branch to hyoglossus muscle.
 LA: Lingual artery.
 HB: Greater cornu of hyoid bone.

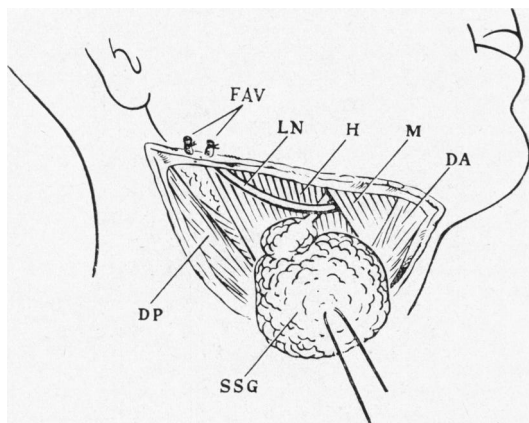


FIG. 3.—The removal of the submandibular gland.

FAV: Facial artery and vein.
 LN: Lingual nerve.
 H: Hypoglossus muscle.
 M: Mylohyoid muscle.
 DA: Digastric anterior belly.
 DP: Digastric posterior belly.
 SSG: Submandibular gland.

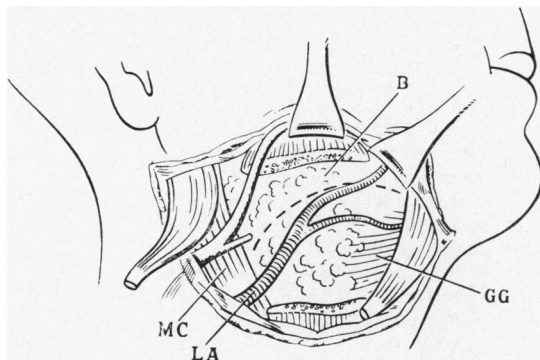


FIG. 5.—The greatly enlarged lingual artery and wall of pharynx after division of the hyoglossus muscle.
 GG: Genioglossus muscle fibres.

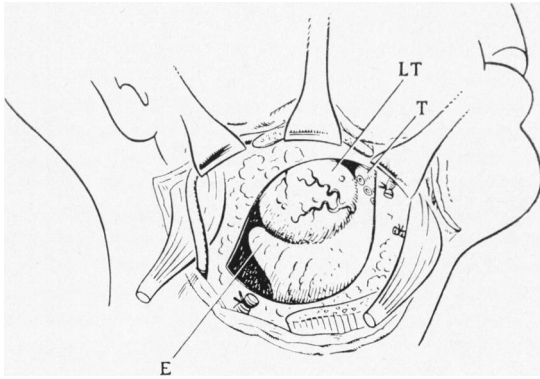


FIG. 6.—The pharynx opened to show the access to area of lingual ectopia.

LT: Lingual thyroid.
T: Tongue (circumvallate papillae).
E: Epiglottis.

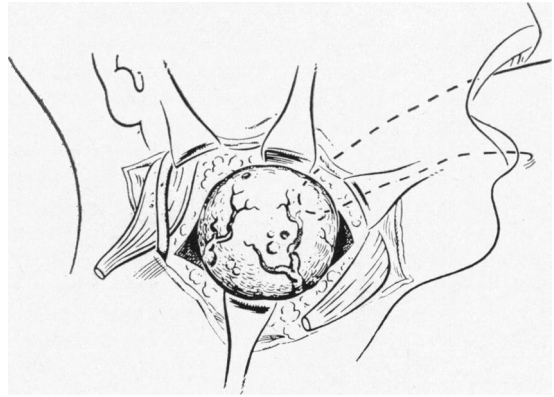


FIG. 7.—The lingual mass displaced into the incision by a finger inserted into the mouth.

injections of 1 ml. were administered intramuscularly at 12-hour intervals and a second P.B.I. estimation of $5.8 \mu\text{g. \%}$ was then obtained. The potency of this preparation was confirmed by a biological assay. The assessment of her thyroid function, based on the first P.B.I. value, was considered to be within normal limits.

The response to T.S.H. showed a low thyroid reserve which must be interpreted in the context of peak pubertal demands. The '48-hour response', a measure of thyroid hormone stored in the gland, was low, which might be expected when estimated during the physiological 'stress' which puberty entails.

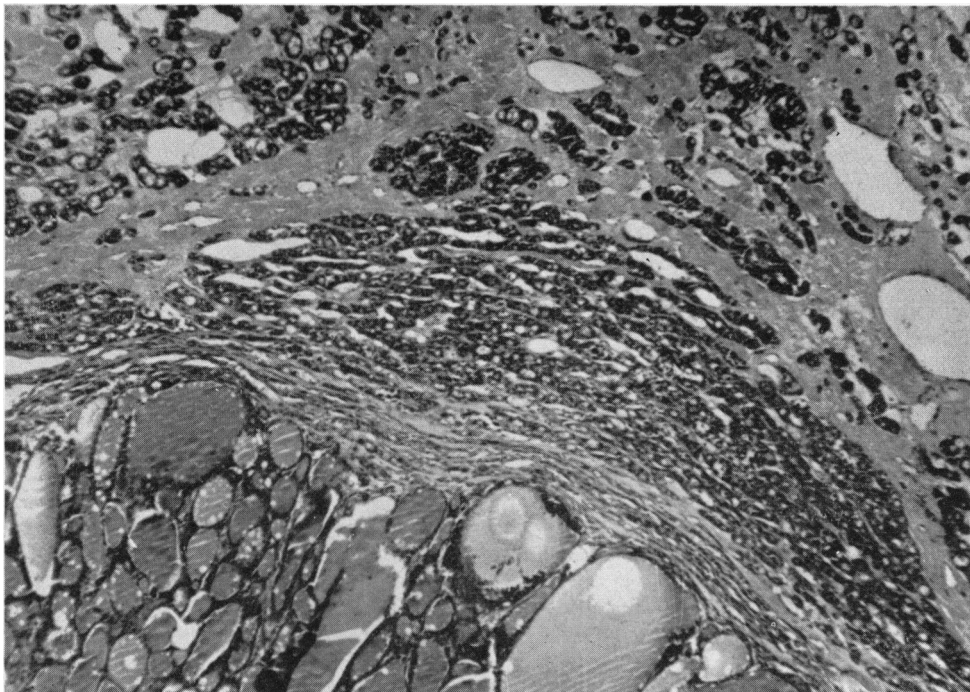


FIG. 8.—Section of the ectopic thyroid mass, showing 'foetal adenoma' pattern which predominated, and an area of colloid vesicle formation below.

Discussion

Embryology. Descriptions of thyroid development differ slightly concerning the median and lateral components. All concur that the median thyroid diverticulum developing from the floor of the embryonic pharynx is a bilobed flask-like structure at the 5-mm. stage. Shortly after the 10-mm. stage each lobe becomes contiguous on its outer side with the ventral components from each fourth pharyngeal pouch. The intimate relationship is accepted, but opinions differ as to how much if any, of the mature thyroid is contributed by the fourth arch (Hamilton, Boyd and Mossman, 1952).

This undetermined factor might account for the coexistence of ectopic thyroid tissue and orthotopic tissue in an individual patient. The situation was more obscure before I^{131} studies were available. Montgomery (1936) concluded that 70% of cases of lingual ectopia had no orthotopic thyroid. More recently Ward, Cantrell and Allan (1954) reported that of eight cases of lingual ectopia investigated with I^{131} , seven showed no orthotopic thyroid present, and the eighth case was probably identical, but documentation was incomplete. It must therefore be assumed that the lingual ectopic thyroid represents the only functioning tissue until I^{131} survey confirms this assumption or, an unlikely event, disproves it.

Indications for Operation. Occasionally lingual ectopia is discovered at necropsy without a history of symptoms and there may well be in the community individuals with asymptomatic thyroid ectopia who never seek treatment. Those with symptoms demand relief and it is they in whom the diagnosis is made and for whom treatment is required. Even if a lingual thyroid mass were an incidental clinical finding, treatment might be necessary to prevent the development of obstructive symptoms and haemorrhage.

Medical measures which have been used include the administration of iodine preparations, and radioactive I^{131} in cytotoxic doses. The former have been unsuccessful in materially reducing the size of the mass, and the latter, by destroying all thyroid tissue present, predicates oral thyroid substitutes.

Early surgical measures such as cautery and multiple circumferential ligature were often incomplete and sometimes fatal. Before thyroid extracts were available they offered a dubious benison; the relief of oropharyngeal symptoms at the price of myxoedema.

Deliberate partial removal of the lingual mass offers no solution. There are theoretical advantages

in leaving sufficient thyroid tissue to maintain normal function while removing the source of obstruction. In practice it is difficult to estimate at operation the amount to be left, and subsequent hyperplasia in response to physiological demands leads to increase in bulk with reappearance of obstructive symptoms (Ackland, 1955).

In the case reported here the concentration of 4.5% μ c. of I^{131} in the tongue five weeks after operation indicates incomplete removal of the ectopic thyroid. The absence of a capsule in this case renders this likely. It is fortunate that secretion in the autograft has been adequate, for if otherwise, the lingual residuum might have attained an appreciable size. Two years after operation the tongue is normal in appearance.

Pathology. Several patterns of cellular arrangement have been observed in lingual ectopia of the thyroid. The commonest is that of a normal thyroid gland, followed next by the 'foetal adenoma' type; colloid and hyperplastic (thyrotoxic) types occur less often.

Almost from the beginning the pathological descriptions have been haunted by the spectre of malignancy arising in the ectopic thyroid tissue, and on the degree of probability of this hinges the permissibility of autotransplantation.

Montgomery (1936) concluded that of eight cases of supposed malignancy in a series of 144, only four warranted serious consideration. He noted that all four occurred in middle-aged males and that no proven case of carcinoma of a lingual thyroid had been reported in the female.

Wapshaw (1942) in a further review reached the same conclusion, the sole exception being one case which was complicated by the presence of orthotopic thyroid tissue with the possibility of neoplasia arising within it.

In the great majority of suspect cases the presumption of malignancy has been based on the microscopic appearances and not on the clinical course.

There are undoubted difficulties in arriving at a correct diagnosis of malignancy in thyroid tissue, which has a well-deserved reputation for being misleading. At one extremity of the morphological spectrum, which carcinoma of the thyroid gland presents, there is a mature and fully differentiated cellular picture, as the discarded terms 'lateral aberrant thyroid' and 'benign metastasizing struma' bear witness. Delay in the appearance of metastasis for decades is well recognized. On the other hand the wild cellular proliferation of some benign hyperplasias may strongly suggest malignancy which is not confirmed by the clinical course.

The frequent absence of a capsule separating the lingual ectopic thyroid tissue from the substance of the tongue is an accepted fact, and the consequent lack of a plane of cleavage leads to the appearance of fragments of thyroid tissue scattered among muscle fibres at the margin of the operative specimen. This has often been misinterpreted as 'capsular invasion' and 'local malignancy'. Subsequent local 'recurrence' after excision of lingual ectopia may well be due to the proliferation of these scattered cells in response to the physiological stimulus of the ensuing hypothyroid state. The embryological development of the thyroid gland and its well-documented anomalies make it likely that fragments of thyroid tissue litter the trail of migration.

The rarity of lingual ectopia, the paucity of long-term follow-up reports and the infrequent attempts at autotransplantation have not provided sufficient evidence hitherto to permit definite conclusions. When all these factors are taken into account the sum of evidence does not appear to be sufficient to prohibit autotransplantation.

Surgery of Access. Several operative approaches have been described. The simplest and most direct is the oral route which has been used since the earliest recorded attempts at surgical relief, the technique evolving from cautery through multiple circumferential ligature to a more precise excision. While some cases lend themselves readily to this approach, others present difficulties which have led to extension of the oral route, to include mandibular osteotomy, incision of the cheek, and splitting of the tongue. These unattractive modifications are avoided by access to the tumour from below the mandible.

Two inframandibular approaches have been described. An anterior suprahyoid or transhyoid pharyngotomy requires a dissection through the body of the tongue (Bocca and Marinoni, 1951). Theoretically the exposure gained is a limited one and has the disadvantage of traversing a vascular organ before reaching the tumour.

Lateral pharyngotomy, first described by Lymphius (1897), has been recorded on six occasions in the literature by Lenzi (1905), Gachet (1912), Owens (1926), Ward *et al.* (1954), and Ackland (1955). In the case presented here lateral pharyngotomy was entirely satisfactory. The exposure was generous and control of half the vessels to the tumour (the right lingual artery and veins) was effected before excision was commenced. The tumour was displaced into the wound and dealt with in full sight. Reconstruction of the strata of the wound was a simple matter and infection due to opening the pharynx was prevented by chemotherapy.

Autotransplantation. Transplantation of the excised thyroid tissue has been attempted in a small number of cases and has met with variable degrees of success. Two cases (Bocca and Marinoni, 1951; Lawson, 1957), have been successful as attested by I^{131} surveys, and a third is reported here. Buckman (1936), Ray (1938), Wapshaw (1942), reported failure in their cases, and Swan, Harper and Christensen (1952), after early promise of success, observed ultimate lack of adequate function in the grafts.

Subsequently Swan *et al.* (1952) conducted a series of laboratory experiments which have contributed greatly to the success of recent attempts. Their conclusions were:

1. The optimal thickness of tissue slices to be grafted is 1-2 mm.
2. The recipient site is relatively unimportant. Muscle and subcutaneous tissue are suitable and accessible.
3. At least two recipient sites should be used, as initial infection and subsequent injury may destroy a single graft.
4. A lag of at least four months is to be expected between implantation and detectable function. The cells of the graft appear normal during this period. Lawson (1960) has noted recurrent swelling and tenderness at the site of the autograft during the menstrual cycle and though this has not yet appeared in the patient whose case is reported here, consideration should be given to this possibility in selecting the donor site; this should take into account all foreseeable fashions in clothing and should not be constricted by an elasticized waist band. The mid-lower portion of the rectus muscle fulfils these desiderata, though the left side might be preferable.

Withholding thyroid preparations during the post-operative phase of hypothyroidism (Stone, Owings and Gey, 1934) is a logical principle. It was originated by Halsted (1909) whose experience in the transplantation of parathyroid glands led him to the intriguing concept that a total lack of the relevant tissue and its secretion was a prerequisite for success in grafting an endocrine gland. Though this theory may not be universally true, it is reasonable to invoke the aid of every factor which could favourably affect the result.

Swan *et al.* (1952), from observations on their patient, thought that thyroid extract administered orally suppressed the thyroid stimulating hormone of the pituitary so that hormone production in the grafts diminished. Further, there was evidence that withdrawal of medication released the pituitary

hormone, resulting in a demonstrable increase in activity in the transplant.

In the present instance, after a period of temporary hypothyroidism the patient showed established activity after a lapse of five weeks, and this appears to be the earliest function yet reported in an autograft. Subsequent investigations corroborate the clinical impression that the patient is euthyroid two years later. Successful transplantation enables the patient to dispense with oral substitution therapy which is always available if the graft should fail.

Summary

A case of lingual ectopia of the thyroid gland, excised and successfully autografted, is reported.

The suggestion is made that the term lingual ectopia be reserved for those cases in which I^{131} survey confirms the absence of orthotopic thyroid tissue.

The clinical picture and recommended investigation are summarized.

The surgical anatomy of lateral pharyngotomy and a technique of autotransplantation are described.

The embryology, pathology, indications for operation, surgery of access, and autotransplantation are discussed.

It is a great pleasure to acknowledge my debt to Mr. Robert Lawson whose encouragement and guidance were freely given. I am also indebted to Dr. Alan Williams for the pathological report and slide preparation, to the Thyroid Clinic of the Royal Melbourne Hospital and the Peter MacCallum Clinic for the scintillometer

reports, to Mr. E. Thake of the Visual Aids Department of the University of Melbourne for the illustrations, and to Dr. Reginald Webster for his help in preparation of the final draft of this paper.

This report and the successful outcome have been due to the generous contributions of an anaesthetist, an endocrinologist, a pathologist, a biochemist, a physicist, an artist and a photographer and typist, and their teamwork is gratefully acknowledged.

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